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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GRUN, JAMES LESLIE	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 06/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/848,390	JOHNSON, LESLIE S.	
	Examiner	Art Unit	
	James L Grun	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *8,17,18,21-26,28 and 29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9-16,19,20 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *09/26/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Technology Center 1600, Group 1640, Art Unit 1641.

Applicant's election with traverse of Group I, claims 1-20 and 27, and the further election of the combination of anti-viral agent with anti-viral antibody in the paper filed 05 November 2003 are acknowledged. The traversal is on the ground(s) that any search of Group II would find the compositions of Group I. This is not found persuasive for the reasons of record indicating the divergent nature of the subject matter as claimed and in view of the overlapping, but not coextensive, searches required.

Claims 21-26, 28, and 29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 8, 17, and 18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species. Examination of claims 14 and 19 with the invention as instantly claimed in claim 1 was not found burdensome by the examiner and, thus, these claims are considered on the merits in this Office action.

The requirement for restriction between the inventions of Groups I and II is still deemed proper and is therefore made FINAL.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

Claims 1-5, 7, 9-11, 13-16, 19, and 20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for combinations of neutralizing anti-respiratory syncytial virus (RSV) F antigen antibodies with anti-viral agents, does not reasonably provide written description and enablement for compositions comprising any and every anti-microbial neutralizing antibody, or undisclosed variants or fragments thereof, with any and every anti-microbial agent. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Other than specific teachings of combinations relevant to RSV infections, applicant provides only general teachings of suggested combinations of agents with a variety of generic activities. The in vivo success of any therapeutic composition is dependent not only upon a particular mode of action but also upon adequate concentrations of drug reaching the desired site of activity. Applicant provides no guidance to other than combinations relevant to RSV infections and no written description or guidance which would allow one to know or predict the function of any other combined agent composition in vivo for treatment of any other disease. There are many

pharmacokinetic properties of drugs such as half-life, deactivation by the liver, binding to plasma proteins, rapid excretion, etc. that would need to be determined and set forth to establish in vivo function for any particular combination for the treatment of any particular disease. Applicant's guidance only to compositions comprising neutralizing anti-RSV antibodies functional for RSV infections does not meet the written description and enablement provisions of 35 U.S.C. 112, first paragraph, for the full breadth of the claims. Moreover, as applicant's specification describes only several particular antibodies and anti-viral agents, applicant provides no guidance to variants or fragments of undisclosed and unknown antibodies which are also functional in the invention. In the absence of any guidance other than to the use of the neutralizing anti-RSV F antigen antibodies, one would not know or be able to predict or envision what structure or modifications were important for function. Therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that a molecule is part of the invention and a reference to a potential method of isolating it. The molecule itself is required. Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of molecules by only their functional activity does not provide an adequate written description of the genus. The court indicated that although applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of molecules falling within the scope of the claimed genus. Applicant is reminded that the written description provision of 35 USC 112 is severable from its

enablement provision. However, in view of the guidance in the instant specification to a single species, the amount of experimentation required to determine functional structures or modifications for other usable species would also be undue. Note that an enabling disclosure for the preparation and use of only a few analogs of a product does not enable all possible analogs where the characteristics of the analogs are unpredictable. See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.* (18 USPQ 2d 1027 (CAFC 1991)).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7, 9-16, 19, 20, and 27 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1-7, 9-16, 19, 20, and 27, the recitations of "including...variants and fragments thereof" are not clear as to what, or how many, antibodies or antibodies including variants or fragments is(are) encompassed within the metes and bounds of the invention.

In claim 6, "the F epitope" lacks antecedent basis.

Claim 15 provides no further limitation of the composition of claim 1 if applicant intended the anti-microbial neutralizing antibody. Alternatively, if applicant intended the agent of claim 1, "said...neutralizing agent" lacks antecedent basis.

Claim 27 is vague and indefinite in the absence of recitation of deposit accession number or other identifying structure or characteristics to clearly identify the antibody because, absent such recitation, it is not clear what structure and properties are encompassed by the named antibodies.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent,
> except that an international application filed under the treaty defined in section 351(a) shall have the effects for the purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language;

Claims 1, 7, 9, 13-15, 19, and 20 are rejected under 35 U.S.C. § 102(e)(2) as being clearly anticipated by Riggs et al. (U.S. Pat. No. 6,110,463).

Riggs et al. teach (see e.g. cols. 13-14) and claim (e.g. claims 5-17) compositions comprising the combination of a neutralizing antibody specific for *Cryptosporidium parvum*, a second antibody specific for another antigen of the parasite, and/or mammalian colostrum which may comprise additional antibodies, including neutralizing antibodies, specific for the parasite.

Claims 1-4, 6, 7, 9-13, 15, and 20 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Crowe et al. (PNAS 91: 1386, 1994).

Crowe et al. teach the delivery of neutralizing anti-respiratory syncytial virus (RSV) F glycoprotein antibodies by aerosol for treatment of RSV infections. The reference teaches that it would be prudent to use a mixture of antibodies directed to different antigenic sites of the virus for treatment to prevent the emergence of antigenic escape mutants of the virus (see e.g. page 1390), thus teaching the compositions as instantly claimed.

Claims 1-4, 6, 7, 9-13, 15, 20, and 27 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Johnson (U.S. Pat. No. 5,824,307).

Johnson teaches neutralizing anti-respiratory syncytial virus (RSV) F antigen antibodies by, inter alia, aerosol for treatment of RSV infections. The reference teaches administration of a plurality of antibodies against the same or different epitopes the RSV F antigen (see e.g. col. 4), thus teaching the compositions as instantly claimed. Inherently, in light of the instant disclosure, the reference teaches the humanized Mab 1129, Medi-493 (see Figs. 7 and 8).

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having

ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

(c) Subject matter developed by another person, which qualifies as prior art only under one or more subsections (e), (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 1-7, 9-13, 15, 16, 20, and 27 rejected under 35 U.S.C. § 103(a) as being unpatentable over Hayden (Antiviral Res. 29: 45, 1996) in view of either of Johnson (U.S. Pat. No. 5,824,307) or Crowe et al. (PNAS 91: 1386, 1994).

Hayden teach combination treatments for respiratory virus infections, including combinations of amantadine with ribavirin, and combinations of neutralizing anti-RSV antibodies with ribavirin. The reference does not teach co-administration of neutralizing anti-RSV antibodies with anti-viral agents in a single composition.

The teachings of Johnson or Crowe et al. are as set forth previously in this Office action.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have provided the combination antiviral therapies of Hayden in a single composition, such as one administered by aerosol, because aerosol delivery of agents to RSV patients, including neutralizing anti-RSV antibodies, is a preferred route of administration as taught in Johnson or Crowe et al., particularly for infants. One would have had obvious motivation to provide a combined treatment in a single composition for convenience and to enhance patient compliance with the treatment.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Johnson et al. (J. Inf. Dis. 176: 1215, 1997) also teaches the humanized anti-respiratory syncytial virus (RSV) F antigen Mab 1129, Medi-493.

Baumann et al. (WO 99/04814) disclose combination compositions of anti-viral antibodies with virostatic agents.

Deen et al. (WO 98/19704) disclose combinations of anti-RSV antibodies for treatment.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, SPE, can be contacted at (571) 272-0823.

The phone numbers for official facsimile transmitted communications to TC 1600, Group 1640, are (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

James L. Grun, Ph.D.
June 24, 2004

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641
6/26/04